I. Remarks

Claims 1 and newly added claims 2-35 are currently pending.

Applicants note that the Office stated that claim 7 was pending in the instant application in the Office Action mailed May 4, 2004. However, it appears that claim 1 was the only claim pending when the Office Action was issued. Applicants do not believe that such an error is material to the rejections set forth in the Office Action but request clarification on this matter nonetheless.

Amendments to the claims:

Claim 1 has been amended by this response. Support for the amendment to claim 1 can be found throughout the instant specification and particularly at page 2, lines 26-31; page 6, lines 27-29; and page 25, lines 14-21. These amendments do not add new matter. Applicants respectfully request their entry.

Claims 2-35 have been added by this response. Support for new claims 2 and 20 can be found throughout the instant specification and particularly at page 26, lines 14-19. Support for new claims 3, 4, 21, and 22 can be found throughout the instant specification and particularly at page 5, lines 21-22; page 26, lines 21-27, and Figures 7, 8, and 9. Support for new claim 5 and 23 can be found throughout the instant specification and particularly at page 8, lines 28-32; page 25, lines 14-2; and Figures 7, 8, and 9. Support for new claim 6-17 and 24-34 can be found throughout the instant specification and particularly at page 8, line 32 - page 9, line 4; and Figure 2. Support for new claim 18 can be found throughout the instant specification and particularly at page 22, lines 8-14; and Figures 4-9. Support for new claim 19 can be found throughout the instant specification and particularly at page 2, lines 26-31; page 6, lines 27-29; and page 25, lines 14-21. . Support for new claims 17 and 35 can be found throughout the instant specification and particularly at page 26, lines 14-19 and Figure 3. These newly added claims do not add new matter. Applicants respectfully request their entry.

Amendments to the specification:

Applicants respectfully requests entry of the amendment to the specification as provided in the section titled "Specification Amendments". These amendments do not add new matter. They correct the brief description of drawings as required by the Office's objections and also bring the instant specification in compliance with the requirements of 37 C.F.R. §1.821 - 1.825 by adding sequence identifiers to the amino acid and nucleic acid sequences contained therein.

Amendments to the drawings:

Applicants respectfully requests entry of the amendment to the drawings as provided in the section titled "Drawing Amendments". These amendments do not add new matter. They correct the drawings to

bring the instant specification in compliance with the requirements of 37 C.F.R. §1.821 - 1.825 by adding sequence identifiers to the amino acid sequences contained therein.

II. Claim rejections under 35 U.S.C. § 112

A) Claim 1 stands rejected under 35 U. S. C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

Applicants assert that the amendments made to claim 1 render this rejection moot. Similarly, this rejection does not apply to newly added claims 2-35. Therefore, withdrawal of this rejection is respectfully requested.

B) Claim 1 stands rejected under 35 U. S. C. 112, first paragraph, because the specification allegedly does not enable the skilled artisan to make and use the invention commensurate in scope with these claims. Applicants respectfully traverse.

Applicants assert that the amendments made to claim 1 render this rejection moot. Similarly, this rejection does not apply to newly added claims 2-35. Therefore, withdrawal of this rejection is respectfully requested.

III. Claim rejections under 35 U.S.C. § 102

Claim 1 stands rejected under 35 USC 102(e) as being allegedly anticipated by High et al. (WO 01/70763 A1, which claims priority to provisional application 60/191,331, filed March 2000.) Applicants respectfully traverse.

High et al. does not and cannot anticipate the instant claims. In the particular embodiment claimed herein, Applicants utilize modified Factor VII polypeptides capable of conversion to activated Factor VII when expressed in an individual. The endogenous Factor VII activation cleavage sequence is mutated to encode for a non-endogenous enzymatic cleavage site capable of being cleaved when expressed intracellularly (see the instant specification at page 6, lines 27-29.) Intracellular cleavage of this polypeptide results in the generation of only a Factor VII heavy chain and a Factor VII light chain. In

contrast, High et al. insert additional amino acid sequences that code for an enzymatic cleavage site into the human Factor VII sequence rather than mutate the endogenous sequence. By utilizing insertion rather than mutation, intracellular cleavage of the High polypeptide results in the generation of a small peptide comprising some portion of the inserted sequence, a Factor VII heavy chain, and a Factor VII light chain. Therefore, High et al. cannot anticipate the instant claims because the methods taught in High utilize different DNA vectors from those of the instant claims and the polypeptides produced by High's methods are different from those of the instant claims as well.

The instant claims utilize modified Factor VII polypeptides capable of conversion to activated Factor VII when expressed in an individual. Applicants create the modified Factor VII by mutating the endogenous Factor VII activation cleavage sequence to encode for a non-endogenous enzymatic cleavage site capable of being cleaved intracellularly. These mutations comprise a modification in the area of about amino acid 147 to about 154 to create an appropriate enzymatic cleavage site. Applicants teach a number of ways to construct these modified Factor VII polypeptides. Such polypeptides, for example, may contain an alteration of the nucleotide sequence of Factor VII such that the proline at position 149 is changed to arginine and the glycine at position 151 is changed to lysine. This mutates the endogenous Factor VII cleavage site to a furin recognition site (see the instant specification at page 8, lines 24-32; page 25, lines 16-21; page 26, lines 21-27.) Other such polypeptides may be created by mutating any one of the amino acids at positions 147-150, 148-151, 150-153, or 151-154 to produce a furin cleavage site such as those of SEQ ID NOS. 17 or 18 (see the instant specification at page 9, lines 1-4; Figure 2.) Applicants further teach that additional Factor VII polypeptides may be created by mutating the endogenous Factor VII cleavage site to an SKI-1 recognition site (see the instant specification at page 26, lines 14-19; Figure 3.) All of these modifications mutate the amino acid sequence from the endogenous cleavage site to an enzymatic cleavage site but do not alter the total number of amino acids with these modifications. Intracellular cleavage of this polypeptide therefore results in the generation of only a Factor VII heavy chain and a Factor VII light chain. In addition, the light chain will necessarily have an amino acid sequences not identical to the endogenous sequences due to the cleavage site mutations introduced by Applicants.

In contrast, High et al. create Factor VII polypeptides by inserting protease cleavage sites, for proteases such as furin, into the endogenous Factor VII activation cleavage sequence (see 60/191,331 at page 2, first full paragraph; page 3, Preliminary data; Figure 1; see WO 01/70763 at page 10, lines 13-22.) They teach three such "amino acid inserts" as examples (see WO 01/70763 at page 35, Example 1.) This insertion necessarily means that the DNA vector of the instant claims is different from the High DNA vector. This insertion also increases the size of the encoded Factor VII polypeptide and results in the generation of three, not two, polypeptides upon enzymatic cleavage. Intracellular cleavage of the High polypeptide will release a small peptide comprising at least a portion of the amino acid insert will be

released along with the heavy and light Factor VII chains (see WO 01/70763 at page 10, lines 13-22.) Therefore, the polypeptides produced upon cleavage of the High polypeptide are different from those of the instant invention as well.

As such, High et al. cannot anticipate the instant claims because the methods and compositions taught in High utilize different DNA vectors from those of the instant claims and the polypeptides produced by High's methods are different from those of the instant claims as well. Therefore, the instant claims are not anticipated because all elements of the instant claims are not provided. For these reasons, Applicants respectfully request withdrawal of this rejection.

VII. Drawing Amendments under 37 C.F.R. § 1.121

Figures 2 and 3 of the instant application have been amended to insert amino acid sequence identifiers (SEQ ID NOS) for each amino acid sequence present into the figures. Such amendment brings the instant specification in compliance with the requirements of 37 C.F.R. §1.821 - 1.825. As such, these amendments do not add new matter. The amended drawings, Figures 2 and 3 are provided as an attachment to this communication labeled "Replacement Sheet".